REMARKS

I. Petition for Extension of Time

Applicants herewith petition the Commissioner for Patents to extend the time for response to the Office action mailed December 22, 2003 for two months from March 22, 2004 to May 22, 2004. Authorization is given to charge the extension of time fee of $420.00 (37 C.F.R. §§1.136 and 1.17) to Deposit Account No. 23-1703. Any deficiency or overpayment should be charged or credited to the above numbered deposit account.

II. Claim Amendment

The claimed invention is directed to an oral pharmaceutical formulation comprising at least one bisphosphonate and one or more additive agents. Claim 1 has been amended to clarify that that the one or more recited additive agents is present in an amount between 80% to 99.9% by weight of the formulation to enhance absorption of the bisphosphonate. Support for the amendment is provided by the specification at page 9, lines 23-25. According, no new matter is introduced by the claim amendment.

III. Claim Rejection – 35 U.S.C. §102

Claims 1-4, 19, 23, 25, 27, 29-34 and 39-46 are rejected for lack of novelty under 35 U.S.C. §102(b) in view of US 5,646,134 to Yates ("Yates"). The Examiner alleges that Yates discloses oral dosage forms comprising a bisphosphonate in combination with the additives of claim 1 for the prevention of bone loss.

Anticipation requires the disclosure of each and every feature of the claimed invention in a single reference. Claim 1, the only independent claim, has been amended to recite that the

recited one or more additive agents is present in an amount between 80% to 99.9% by weight of the formulation to enhance absorption of the bisphosphonate.

Paragraph 21 of Yates provides the only disclosure of an actual oral dosage form. None of the examples provided by Paragraph 21 discloses an oral dosage form comprising any of the recited additives of claim 1 in an amount between 80% to 99.9% by weight of the formulation. Accordingly, Yates fails to disclose each and every feature of the claimed invention.

Withdrawal of the §102 rejection is requested.

IV. Claim Rejection – 35 U.S.C. §103

Claims 5, 10, 11, 15, 16, 20, 22, 24, 26, 28 and 47 are rejected for obviousness reasons under 35 U.S.C. §103 in view of Yates. The Examiner notes that Yates does not disclose the additives of the rejected claims. However , it is alleged that it would have been obvious to one skilled in the art to substitute one pharmaceutically acceptable additive for another.

Applicants respectfully submit that the issue of patentability is not merely whether one additive can be substituted for another in combination with a bisphosphonate to formulate a dosage form for the treatment and prevention of osteoporosis. Rather, it is Applicants' invention that the one or more additive agents of claim 1 is present in an amount sufficient to provide enhanced absorption of orally administered bisphosphonate. Amended claim 1 clarifies that the amount of the additive sufficient to enhance absorption of orally administered bisphosphonate is between 80% to 99.9% by weight of the formulation.

As discussed in Section III, above, none of the examples provided by Yates discloses an oral dosage form comprising any of the recited additives of claim 1 in an amount between 80% to 99.9% by weight of the formulation. Nor is there any suggestion of the recited range. This is

not surprising since Yates does not recognize the problems associated with the oral administration of bisphosphonates. As such, there no appreciation of the need or means for enhancing the absorption of orally administered bisphosphonate.

Rather, the objective of Yates is to retard the loosening of an orthopedic implant device by the administration of a bisphosphonate by any of the alternative methods disclosed by Yates. For example, Yates discloses that the bisphosphonate may be administered orally or parenterally (See Paragraph 11). Alternatively, the bisphosphonate may be implanted directly at the site to be treated or by coating the implant device with the bisphosphonate (See Paragraphs 14 and 15). Thus, the object of Yates is achieved by the administration of a bisphosphonate in an osteogenically effective amount by any of the disclosed methods without any regard for enhancing the absorption of orally administered bisphosphonate (See Paragraph 4).

The Examiner's attention is directed to WO 88/00829 which was previously cited in support of claim rejections under 35 U.S.C. §§102 and 103. All of these claims rejections have been withdrawn. The publication WO 88/00829 describes the disadvantages associated with the oral administration of bisphosphonates. The following disclosure appears at page 1, lines 13-20 of WO 88/00829:

> Bisphosphonates have hitherto been administered either orally or intravenously to patients. ***However, the oral absorption is poor and often accompanied by gastrointestinal side effects. Furthermore, the degree of absorption shows substantial individual variations.*** Consequently, intravenous administration has up till now had to be used whenever a rapid and reliable delivery of bisphosphonates was needed. (Emphasis added)

Yates is concerned with the administration of a bisphosphonate in an osteogenically effective amount (See Paragraph 4). As such, Yates is no different from the prior art as represented by WO 88/00829 which discloses that it was known to administer bisphosphonates

orally to patients. However, neither WO 88/00829 nor Yates discloses or suggests a solution for enhancing the absorption of bisphosphonates when administered orally. In this regard, Applicants submit that the administration of "***an osteogenically effective amount***" of a bisphosphonate by any of the methods disclosed by Yates is patentably different from the administration of a bisphosphonate and one or more additives in "***an amount between 80% to 99.9% by weight of the formulation to provide an enhanced absorption of the bisphosphonate***" as required by the claimed invention.

The patentable invention lies in the discovery that absorption of orally administered bisphosphonate is enhanced when the one or more additive agents of claim 1 is present in an amount sufficient to provide enhanced absorption of the bishosphonate. Amended claim 1 clarifies that the amount of the additive sufficient to enhance absorption of the bisphosphonate is between 80% to 99.9% by weight of the formulation. Yates does not recognize the problem with absorption of the bisphosphonate or the solution.

For all of the foregoing reasons, the Examiner has failed to establish a *prima facie* case of obviousness. Withdrawal of the §103 rejection is therefore requested.

CONCLUSION

Applicants submit that pending claims 1-21, 23-34, 40-42 and 45-47 are in condition for allowance, which action is earnestly solicited. The Assistant Commissioner is hereby authorized to charge Deposit Account No. 23-1703 in the event that any fee is required in connection with this communication.

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Respectfully submitted,

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